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# Biominéralisation
# &
# Pathologies µcritallines - Les dépôts anormaux dans le corps humain

# La belle et la bête


**D. Bazin[a], M. Daudon[b,c], J.P. Haymann[b,c], E. Letavernier[b,c], V. Frochot[b,c]**

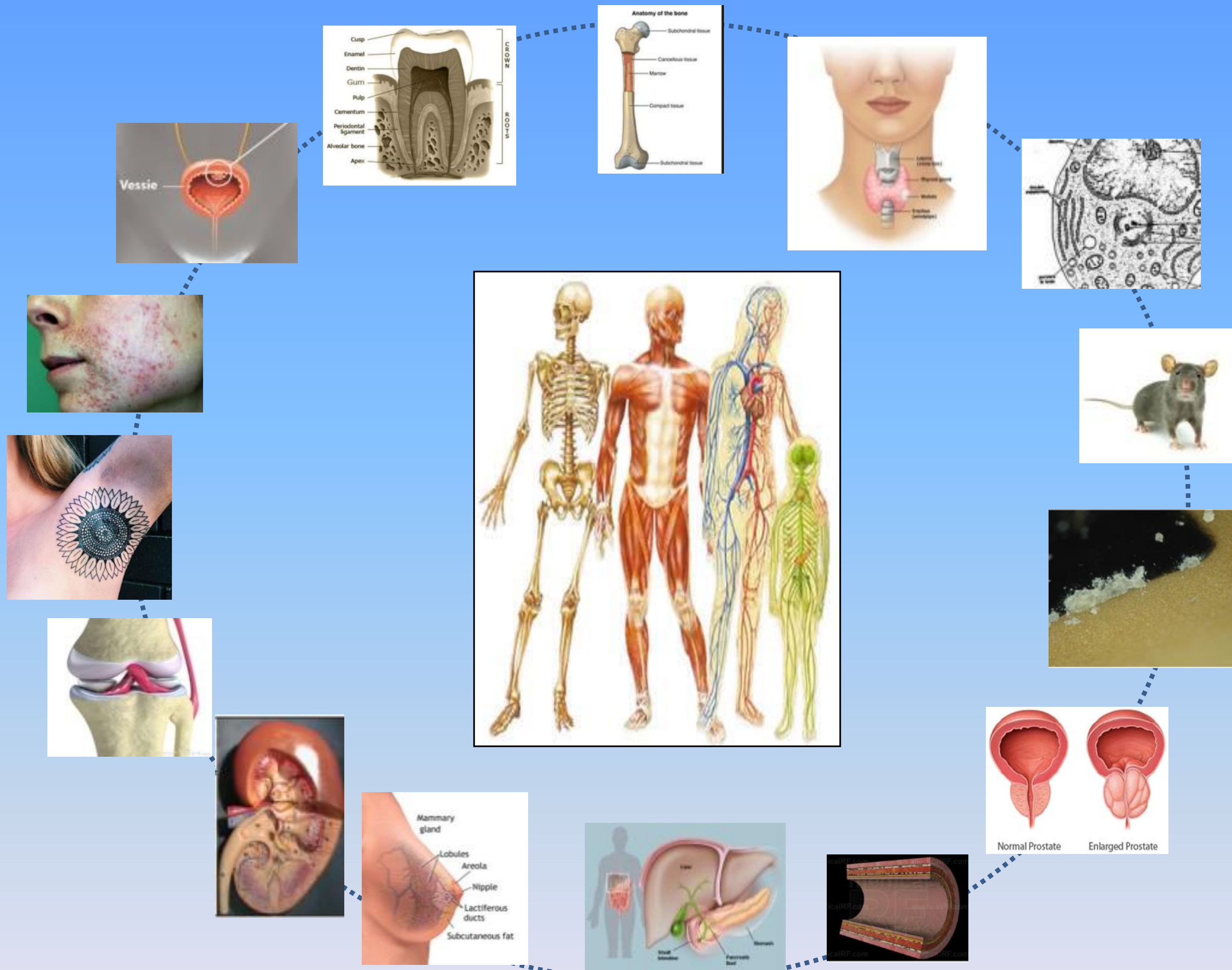
LCP

**[a]LCP, Université Paris XI.**
**[b] Inserm, UMRS 1155, UPMC, Hôpital Tenon.**
**[c] Service des explorations fonctionnelles, Hôpital Tenon.**

Hôpitaux Universitaires Est Parisien
TENON

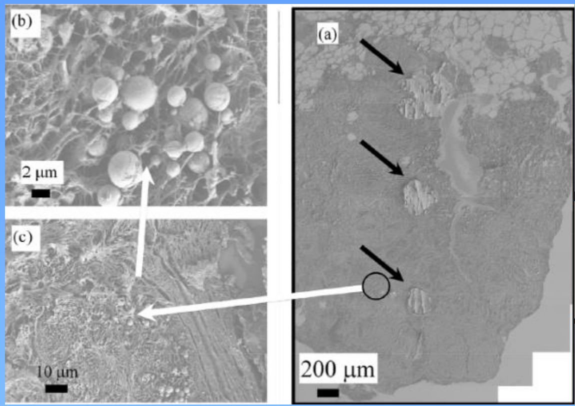


- *Bazin D., Daudon M., Combes Ch., Rey Ch., Characterization and some physicochemical aspects of pathological microcalcifications, Chem. Rev. 112 (2012) 5092.*
- Bazin D., Daudon M., Les pathologies microcristallines et les techniques de physicochimie : quelques avancées, Ann. Biol. Clin. 73(2015)517.




- Calcifications pathologiques : un diagnostic médical basé sur leurs paramètres physicochimiques, Bazin D., Haymann J.-Ph., Letavernier E., Rode J., Daudon M., Presse Médicale 43(2014)135.

53 références dans pubmed « Bazin & Daudon – auteurs »; (116 sur Web of Science, Nbcitations > 1274 sur WoS).

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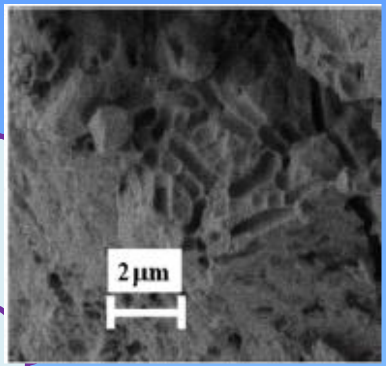
Cancer

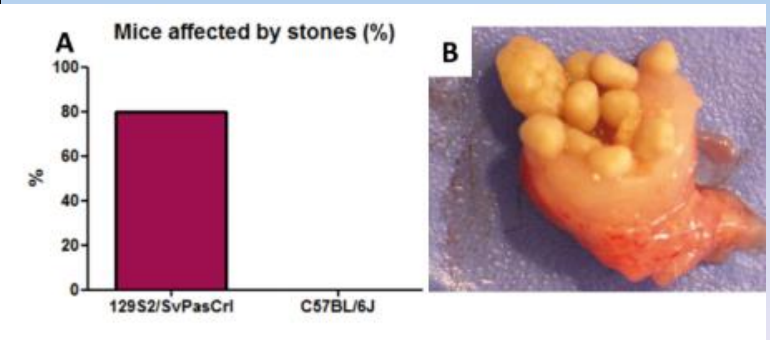
Infection



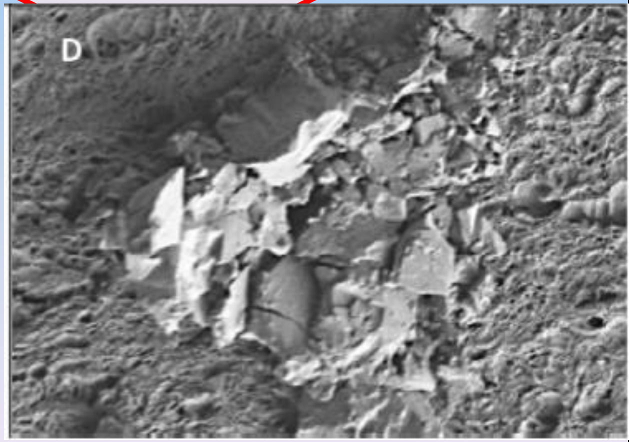

Calcifications Pathologiques

Maladie Génétique

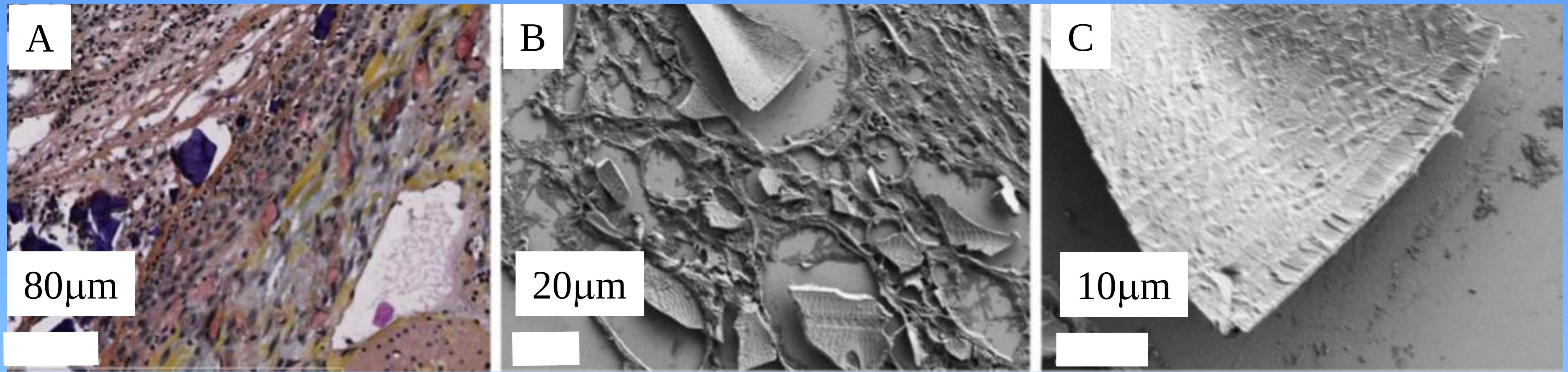
Maladie Cardiovasculaire




*Livrozet M. et al., PLoS ONE 9 (2014)e102700.*

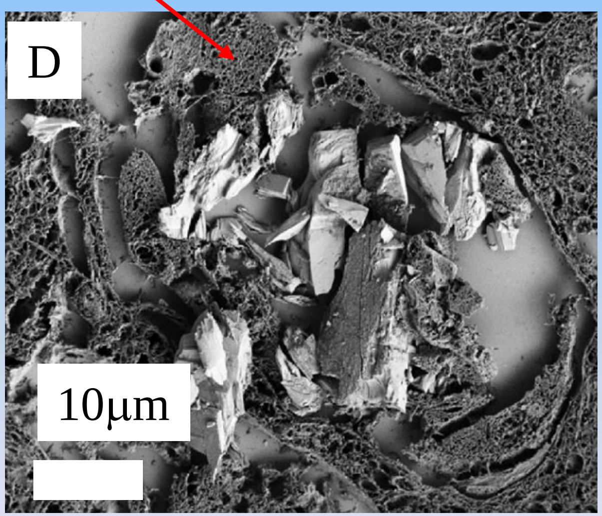


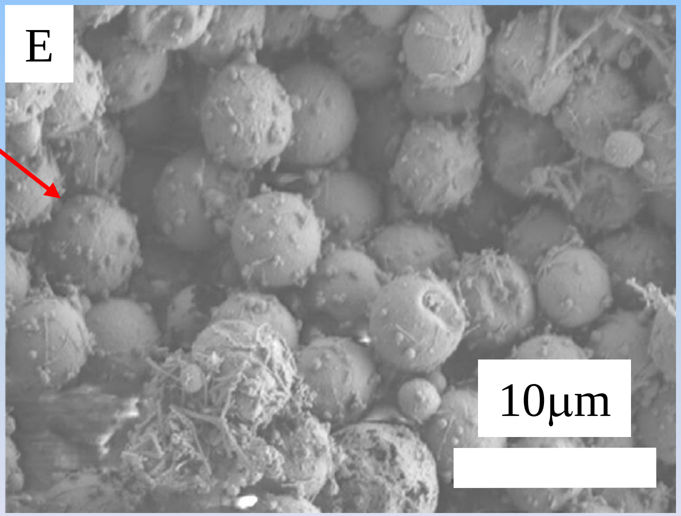

*Coscas R. et al., Atherosclerosis 259(2017)60*




*CP d'origine exogène – engendrant la pathologie (A,B,C) cristaux de sulfonate de polystyrène sodique*

*(D) cristallites de foscarnet,* *(E) sphères de silice présentes dans un calcul rénal du Burkina-Faso.*



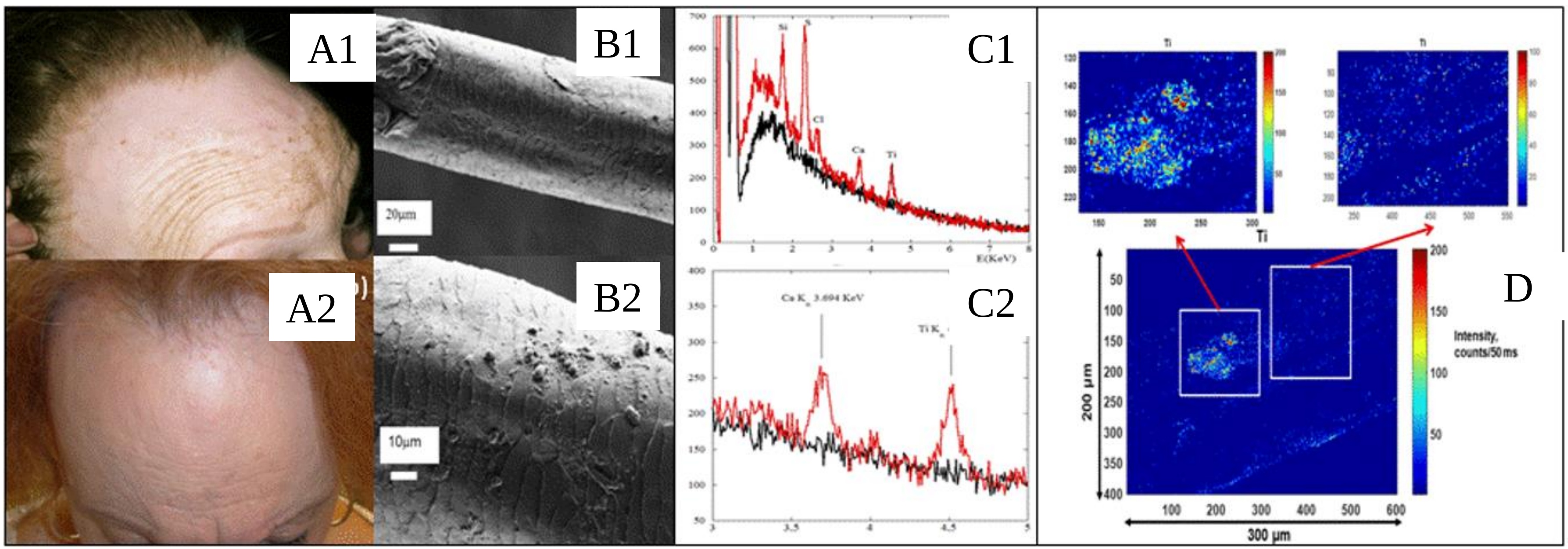

Daudon M. et al., The Lancet 349(1997)1294
Daudon M. et al., Drugs 64(2004)245.
Frochot V. et al., C.R.Ch.Acad.Sci. 19(2016)1565.
Daudon M. et al. Drugs. 78(**2018**)163.

Maurice-Estepa L. et al., A.J.K.D. 32(1998)392.
Dessombz A. et al., Urology 86(2015)1090.
Luque Y. et al., J. Am. Soc. Nephrol. 28(**2017**)1669.
Faucon A.L. et al., Kidney Int. 93(**2018**)1251.

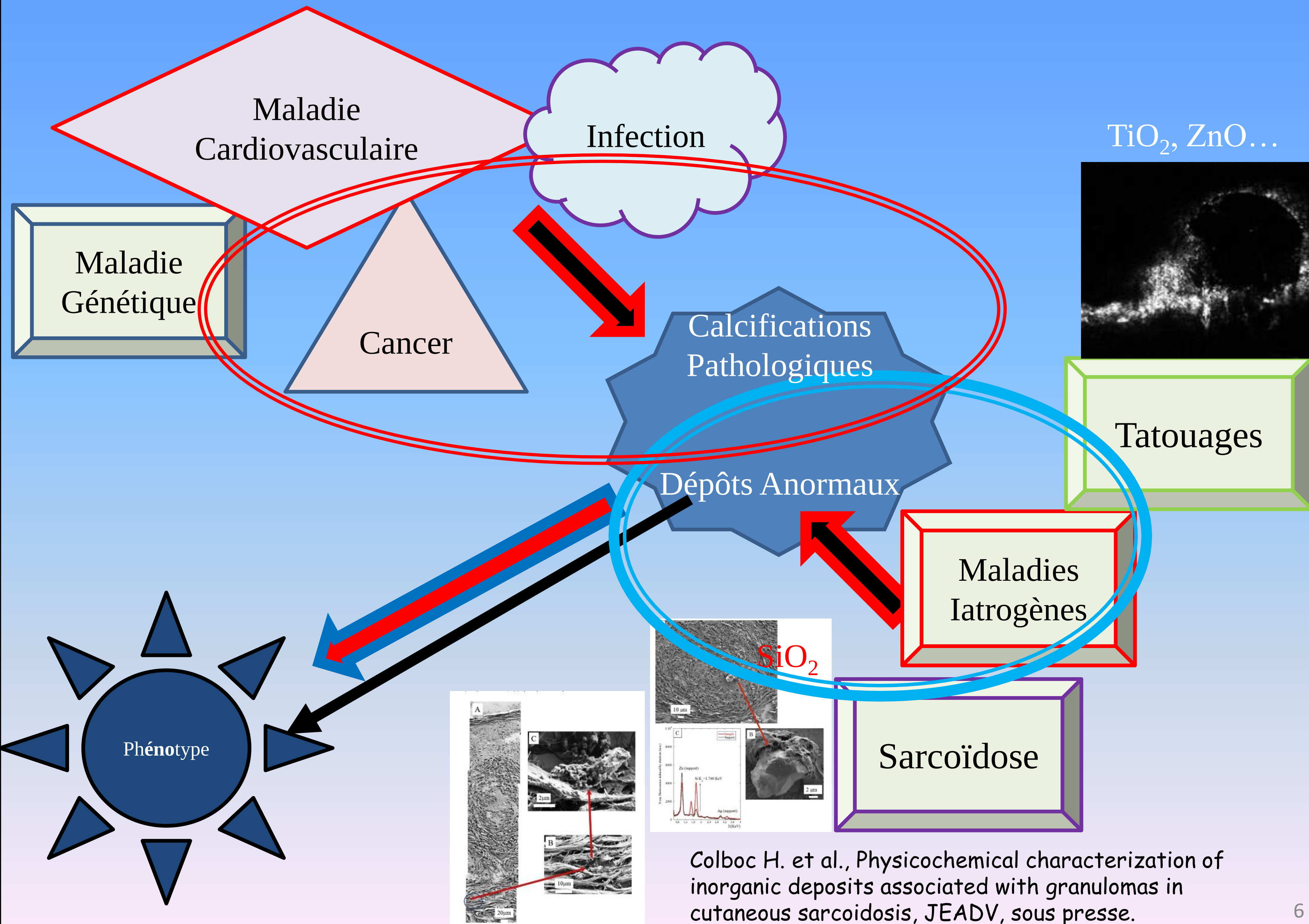
# Detection of titanium nanoparticles in the hair shafts of a patient with frontal fibrosing alopecia

F. Brunet-Possenti,[1,*] L. Deschamps,[2] H. Colboc,[3] A. Somogyi,[4] K. Medjoubi,[4] D. Bazin,[5] V. Descamps[1]

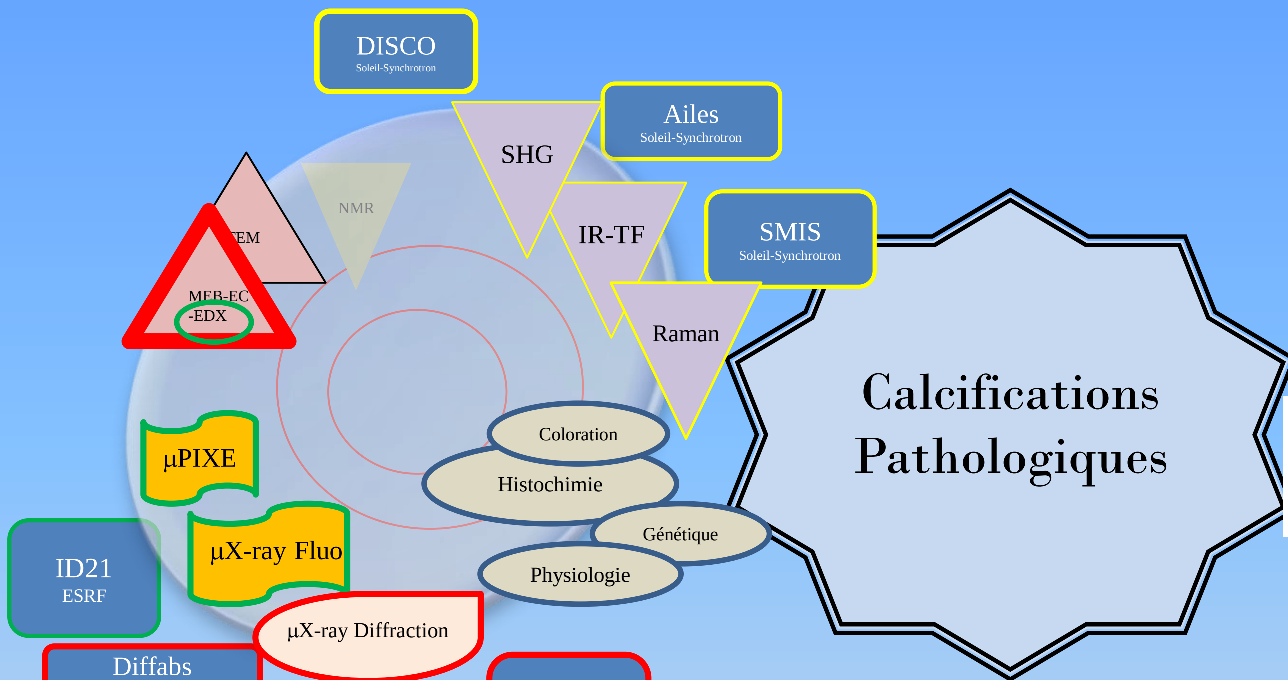
[1]Department of Dermatology, Bichat Hospital, HUPNVS, AP-HP, Paris 7 University, Paris, France, [2]Department of Pathology, Bichat Hospital, HUPNVS, AP-HP, Paris, France, [3]Department of Dermatology, Rothschild Hospital, AP-HP, Paris, France, [4]Synchrotron SOLEIL, Gif-sur-Yvette, France, [5]LCMCP-UPMC, College de France, Paris, France

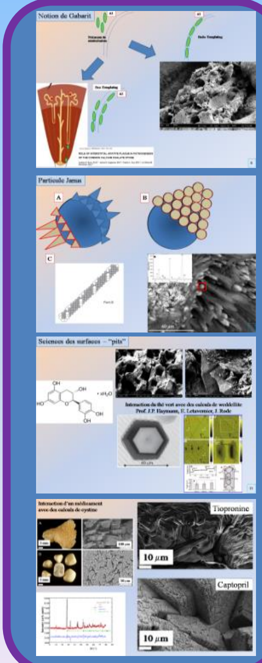



Brunet-Possenti F. et al., J Eur Acad Dermatol Venereol. 32(2018)e442.




Colboc H. et al., Physicochemical characterization of inorganic deposits associated with granulomas in cutaneous sarcoidosis, JEADV, sous presse.



## Description de leurs caractéristiques physicochimiques

- ❖ Relation entre la calcification et la pathologie: simple proximité spatiale ou relation de causalité ?
- ➢ Définir les paramètres biochimiques responsables de leur pathogénèse
- ✓ Développer de nouveaux outils de diagnostic

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Journal of Trace Elements in Medicine and Biology 27 (2013) 326–333

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EPIDEMIOLOGY

# Combining μX-ray fluorescence, μXANES and μXRD to shed light on $Zn^{2+}$ cations in cartilage and meniscus calcifications

Arnaud Dessombz[a], Christelle Nguyen[b,c,d,e], Hang-Korng Ea[b,c,f], Stephan Rouzière[a], Eddy Foy[g], Didier Hannouche[d,e,c], Solene Réguer[h], Frederic-Emmanuel Picca[h], Dominique Thiaudière[h], Frédéric Lioté[b,c,f], Michel Daudon[i], Dominique Bazin[j,*]

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[b] INSERM, UMR-S 606, Hop. Lariboisière, Paris, France
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[d] AP-HP, Orthopaedic Surgery Department, Pôle Appareil Locomoteur, Hop. Lariboisière, Paris, France
[e] CNRS, UMR 7052, Paris, France
[f] AP-HP, Lariboisière Hospital, Rheumatology Department, Centre Viggo Petersen, Pôle Appareil Locomoteur, Paris, France
[g] LAPA SIS2M, CEA/CNRS UMR 3299, CEA Saclay, Gif sur Yvette Cedex, France
[h] Synchrotron SOLEIL, L'Orme des Merisiers, Saint-Aubin, Gif-sur-Yvette, France
[i] AP-HP, Tenon Hospital, Service d'explorations fonctionnelles, 4 rue de la Chine, Paris, France
[j] Laboratoire de Chimie de la Matière Condensée de Paris, Université Pierre et Marie Curie et Collège de France, 11 place Marcelin Berthelot, Paris, France

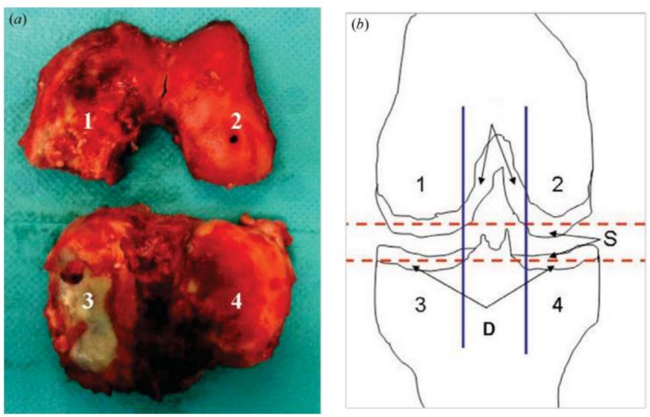



**Figure 1**
Knee joint specimen obtained during arthroplasty and schematic representation of the sample collection protocol. The specimen included femoral condyle and tibial plateau cartilage from both the medial and the lateral compartments (*a*). Cartilage areas were labelled as follows: 1, medial condyle; 2, lateral condyle; 3, medial tibial plateau; 4, lateral tibial plateau; S, superficial layer; D, deep layer (*b*).





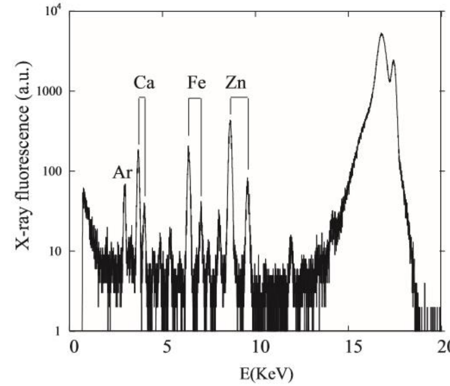



**Fig. 1.** Representative X-ray fluorescence (XRF) spectra: contributions of Ar ($K_\alpha$ = 2958 eV), Ca ($K_\alpha$ = 3691 eV, $K_\beta$ = 4012 eV), Fe ($K_\alpha$ = 6404 eV, $K_\beta$ = 7058 eV) and Zn ($K_\alpha$ = 8638 eV, $K_\beta$ = 9572 eV).

Finally, all samples were characterized by use of FTIR spectrometry (Vector 22; Brucker Spectrospin, Wissembourg, France) as described [30]. Data were collected in the absorption mode between 4000 and 400 $cm^{-1}$, with resolution 4 $cm^{-1}$. We used previous assignments of absorption bands [30]. Regarding carbonated apatite [CA; $Ca_{10}(PO_4)_6(OH)_x(CO_3)_y$], the $\nu_1$ and $\nu_3$ P—O stretching vibration modes were measured at 960–962 $cm^{-1}$ and 1035–1045 $cm^{-1}$ respectively, and the O—P—O $\nu_4$ bending mode corresponded to the doublet at 602–563 $cm^{-1}$. Regarding m-CPPD, O—P—O bending was recorded at 535 and 508 $cm^{-1}$. P—O symmetric stretching vibrations generated absorption at 923 and 991 $cm^{-1}$, and asymmetric stretching vibrations generated absorption at 1037 and 1089 $cm^{-1}$.

## Results

Representative μXRF spectra are in Fig. 1. The contributions of Ca, Fe and Zn (contribution of Ar is due to the experiments being performed in air) are clearly observed. From this μX-ray fluorescence spectrum, the spatial distribution of Ca and Zn were built for the samples HC69 (Fig. 2A), HC72 (Fig. 2B), MEM1 (Fig. 3A) and MEM2 (Fig. 3B). At the mesoscopic scale, the spatial distribution of Ca and Zn is heterogeneous, which indicates the presence of μcalcifications. Moreover, the Zn-rich parts of the samples were not always on the calcification. Note that the average Zn content is 48.1 ± 4.2 ppm.

Various XANES spectra were acquired at the Zn K-absorption edge corresponding to the different positions indicated on the Zn maps to determine the Zn atom environment of the samples HC69 and HC72 (Fig. 4) and MEM1 and MEM2 (Fig. 5). The spectra for samples HC69 and HC72 (Fig. 4) are all similar and different from those for the 2 reference compounds, namely smithsonite and zincite

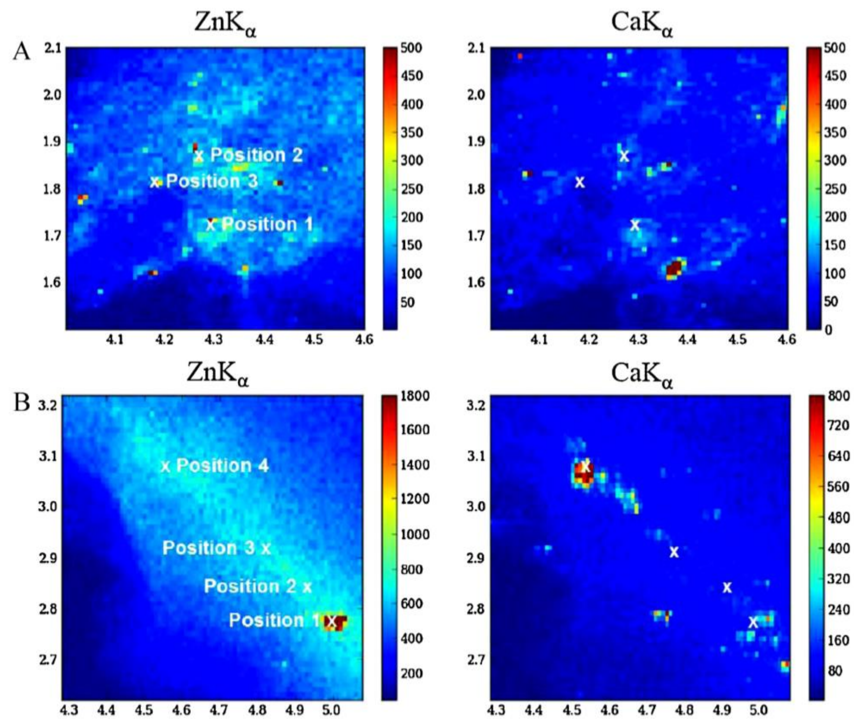



**Fig. 2.** Microanalysis XRF maps of Zn and Ca in human cartilage (HC) samples HC69 (A) and HC72 (B). Position 1 is a hot-point, probably a pollutant, and would be eliminated.

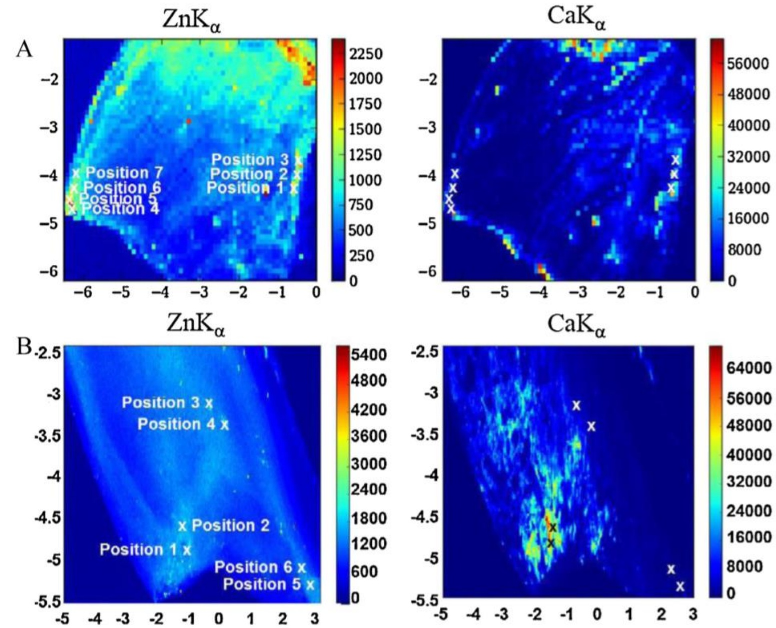



**Fig. 3.** μXRF maps of Zn and Ca in medial miniscus (MEM) samples MEM1 (A) and MEM 2 (B).

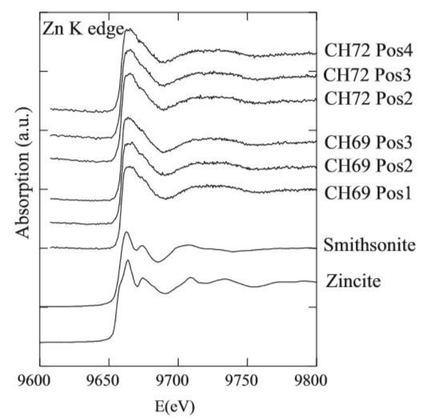



**Fig. 4.** Microanalysis X-ray absorption near edge structure (μXANES) spectra recorded at the Zn K edge for CH69 and CH72 samples and 2 reference compounds (smithsonite and zincite).

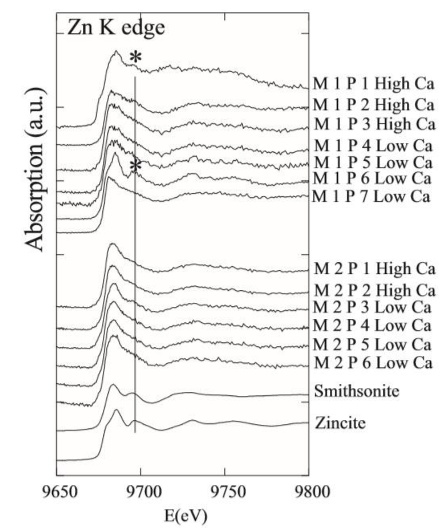
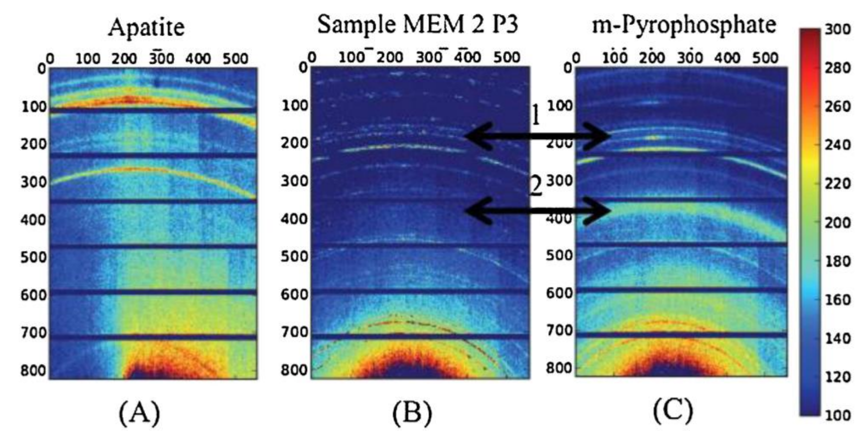
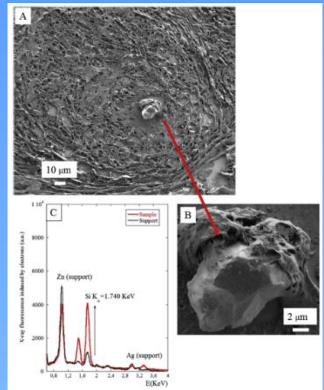


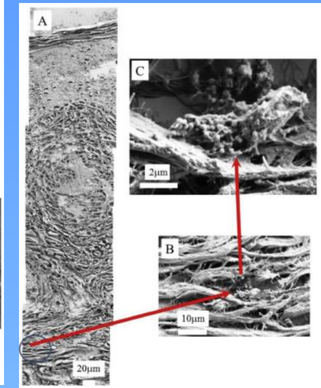

**Fig. 5.** μXANES spectra recorded at the Zn K edge for meniscus samples (MEM1 and MEM2) and 2 reference compounds (smithsonite and zincite).



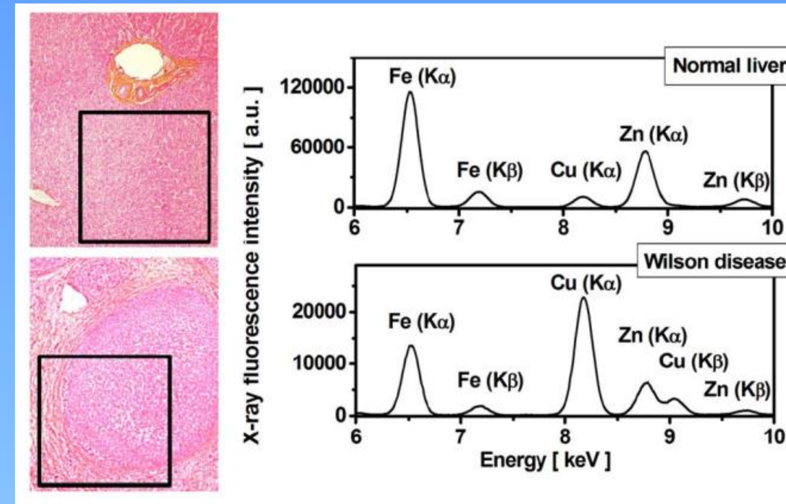



roanalysis X-ray diffraction (μXRD) diagrams for the reference compounds (apatite and monoclinic-pyrophosphate) and the sample MEM2 by the XPAD d

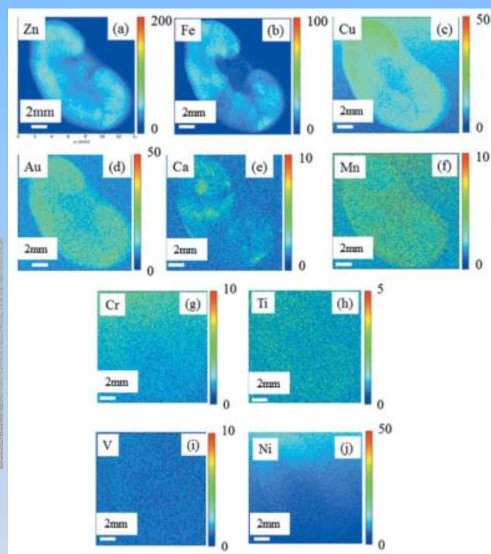


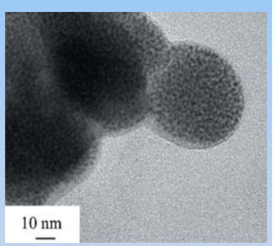




H. Colboc *et al.*,
C.R. Chimie 2016

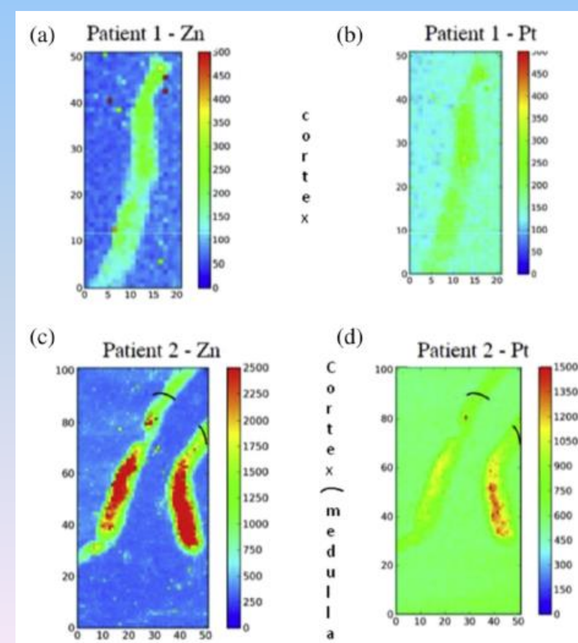



S. Kascakova *et al.*,
The Journal of Pathology: Clinical Research, 2016

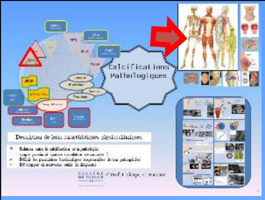



E. Esteve *et al.*,
J Syn. Rad., 2017




E. Esteve *et al.*,
C.R. Chimie 2016



# type I calcium oxalate; tumeurs bénignes
# type II hydroxyapatite, tumeurs bénignes ou malignes..

## Carbonatation de l'apatite

R Baker, K D Rogers, N Shepherd, N Stone relationships between breast µcalcifications and cancer, *British J. of Cancer* 103 (2010) 1034

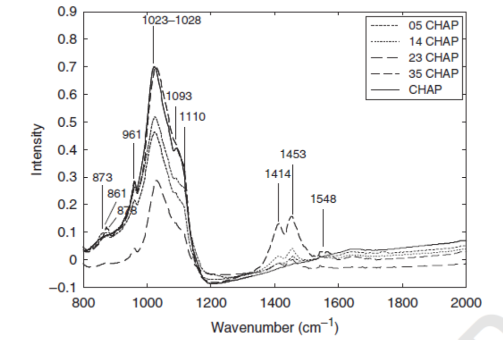
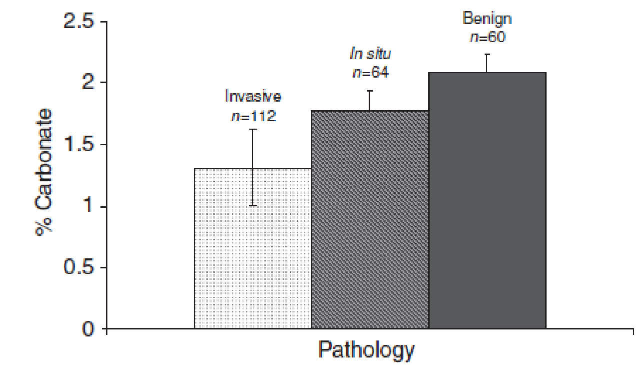



**Figure 2** Mean spectrum from each CHAP standard ranging from 0 to 3.5% carbonate substitution.




## Morphologie

*American Mineralogist, Volume 83, pages 1122–1126, 1998*

LETTERS

**Using scanning electron microscopy to study mineral deposits in breast tissues**


SARAH HOUGEN POGGI,[1] H. CATHERINE W. SKINNER,[2,*] JAY J. AGUE,[3] AND DARRYL CARTER[4]

[1]Department of Obstetrics and Gynecology, School of Medicine, University of California, Los Angeles, California 90095, U.S.A.
[2]Departments of Geology and Geophysics, Yale University, and Orthopaedics and Rehabilitation, Yale University School of Medicine, New Haven, Connecticut 06520, U.S.A.
[3]Department of Geology and Geophysics, Yale University, New Haven, Connecticut 06520, U.S.A.
[4]Department of Pathology, Yale University School of Medicine, New Haven, Connecticut 06520, U.S.A.

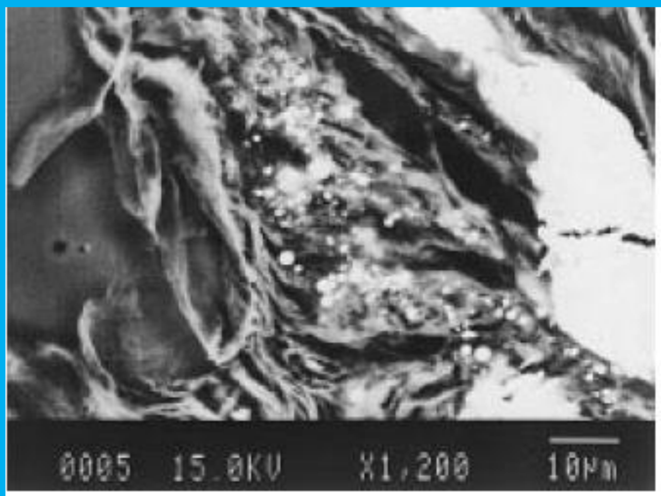
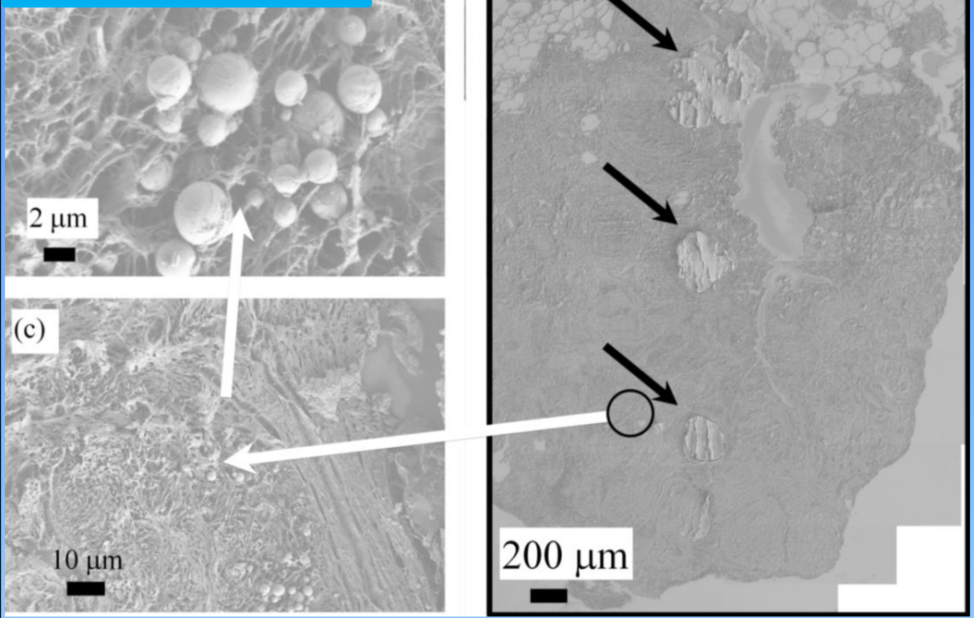




FIGURE 3. SEM-BSE photo of calcium phosphate spherules in stromal tissue (fibroadenoma). Note the bimodal size distribution of spherules in the center of the photo relative to the heavily mineralized deposit of calcium phosphate on the right. Histological section, 6 mm thick, of breast tissue.

# Morphologie




# Agglomération des sphères générant des macrocalcifications

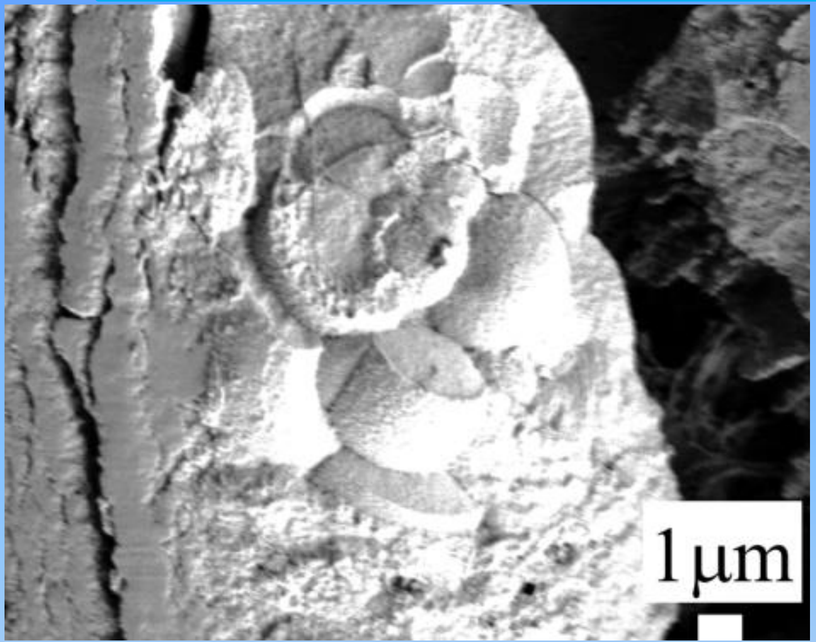
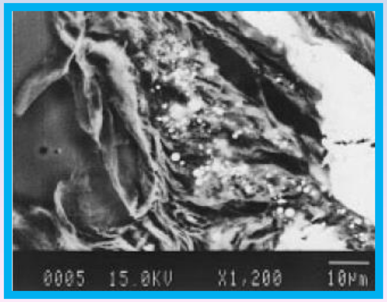
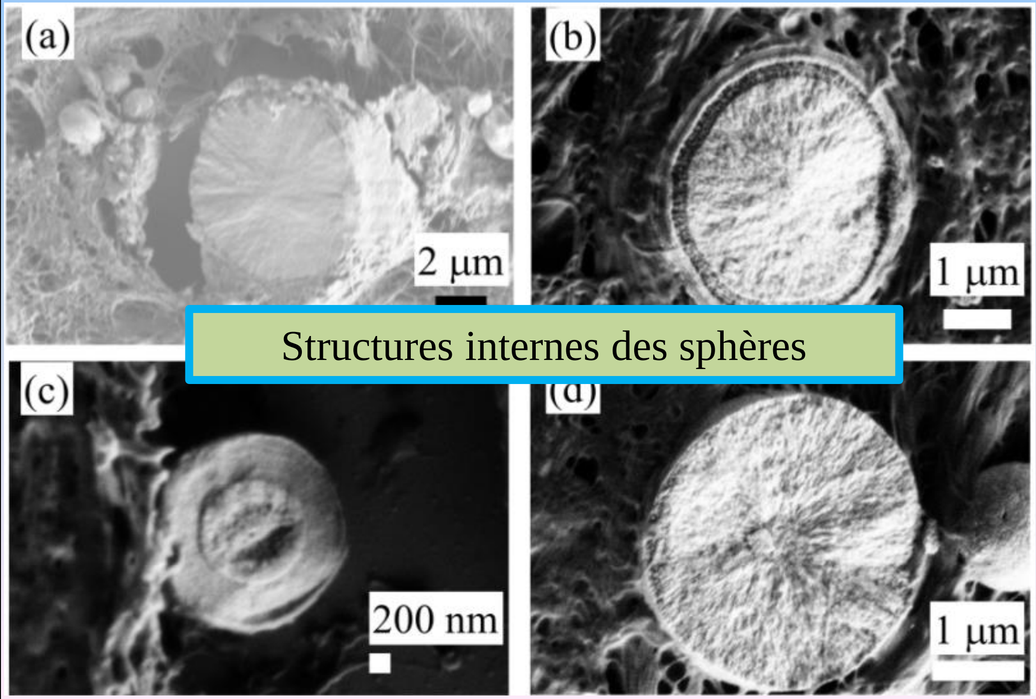


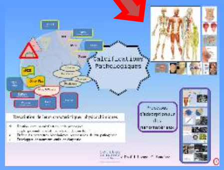

**Table 1**
Physiological and clinical data of the first set of samples.

| Sample | Age (years) | Disease |
|---|---|---|
| Sample A – 13H2480 | 65 | Normal breast (duct) |
| Sample B – 13H2606 | 60 | Fibroadenoma |
| Sample C – 13H2282 | 61 | Galactophoric cyst |
| Sample D – 13H2427 | 57 | Adenosis |
| Sample E –13H2281 | 62 | Ductal carcinoma in situ (DCIS) |



# Structures internes des sphères

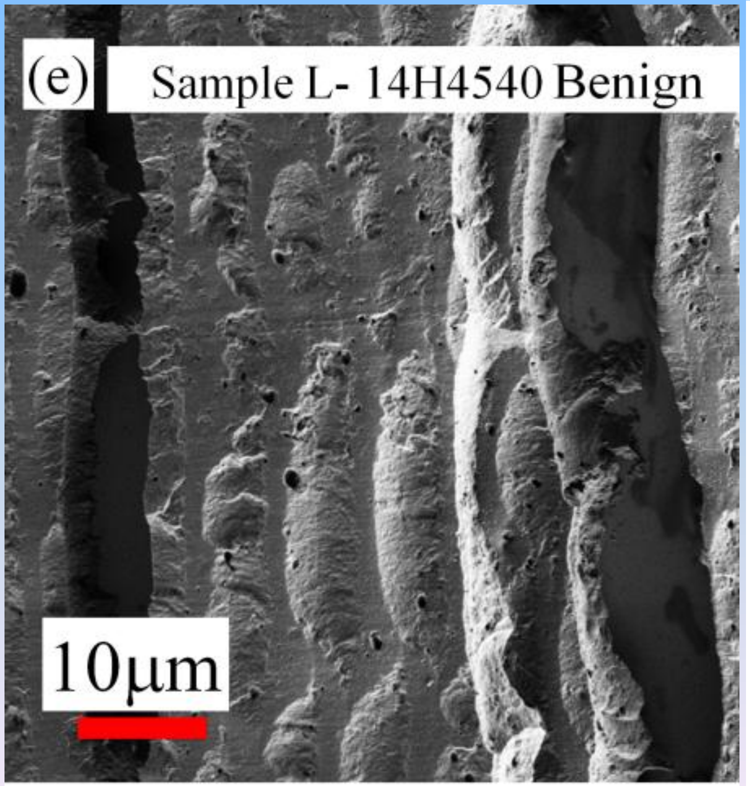


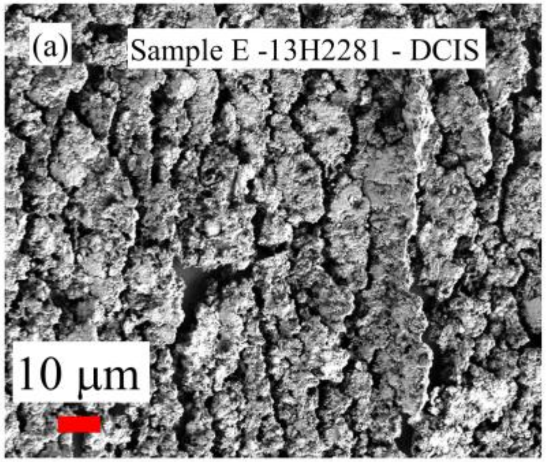


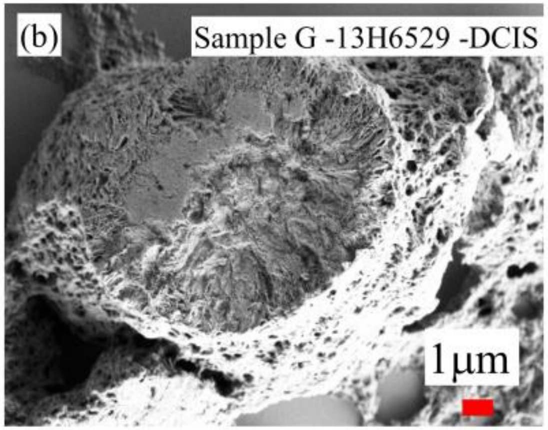
# Morphologie
# tumeurs bénignes ou malignes (DCIS)????

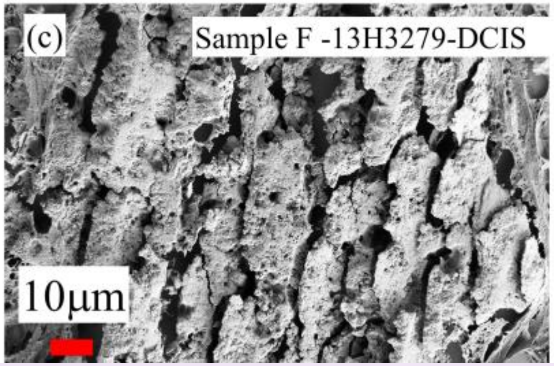
**Table 2**
Physiological and clinical data of the second set of samples.

| Sample | Age (years) | Disease |
|---|---|---|
| Sample F – 13H3279 | 60 | DCIS |
| Sample G – 13H6529 | 55 | DCIS |
| Sample H – 13H2851 | 66 | DCIS |
| Sample I – 13H1096 | 70 | DCIS |
| Sample J – 13H8746 | 66 | DCIS |
| Sample K – 14H2554 | 37 | Benign |
| Sample L – 14H4540 | 50 | Benign |
| Sample M – 13H4111 | 63 | Benign |

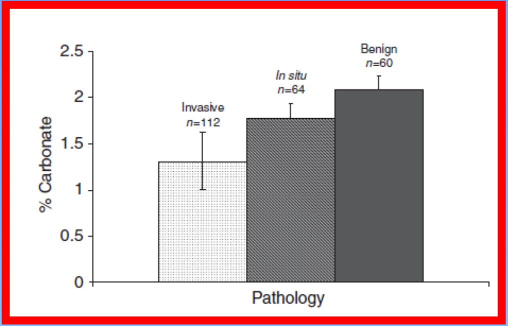


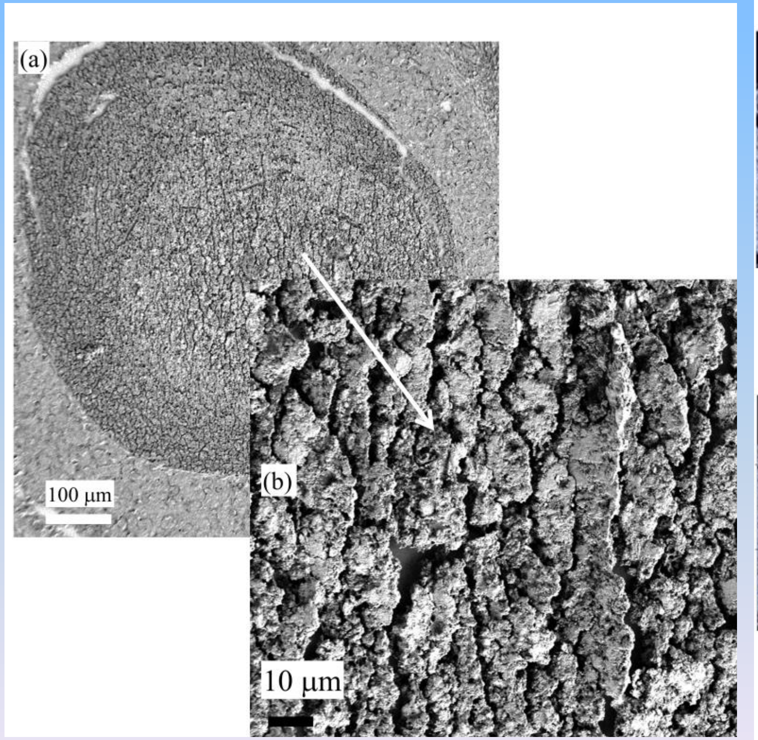



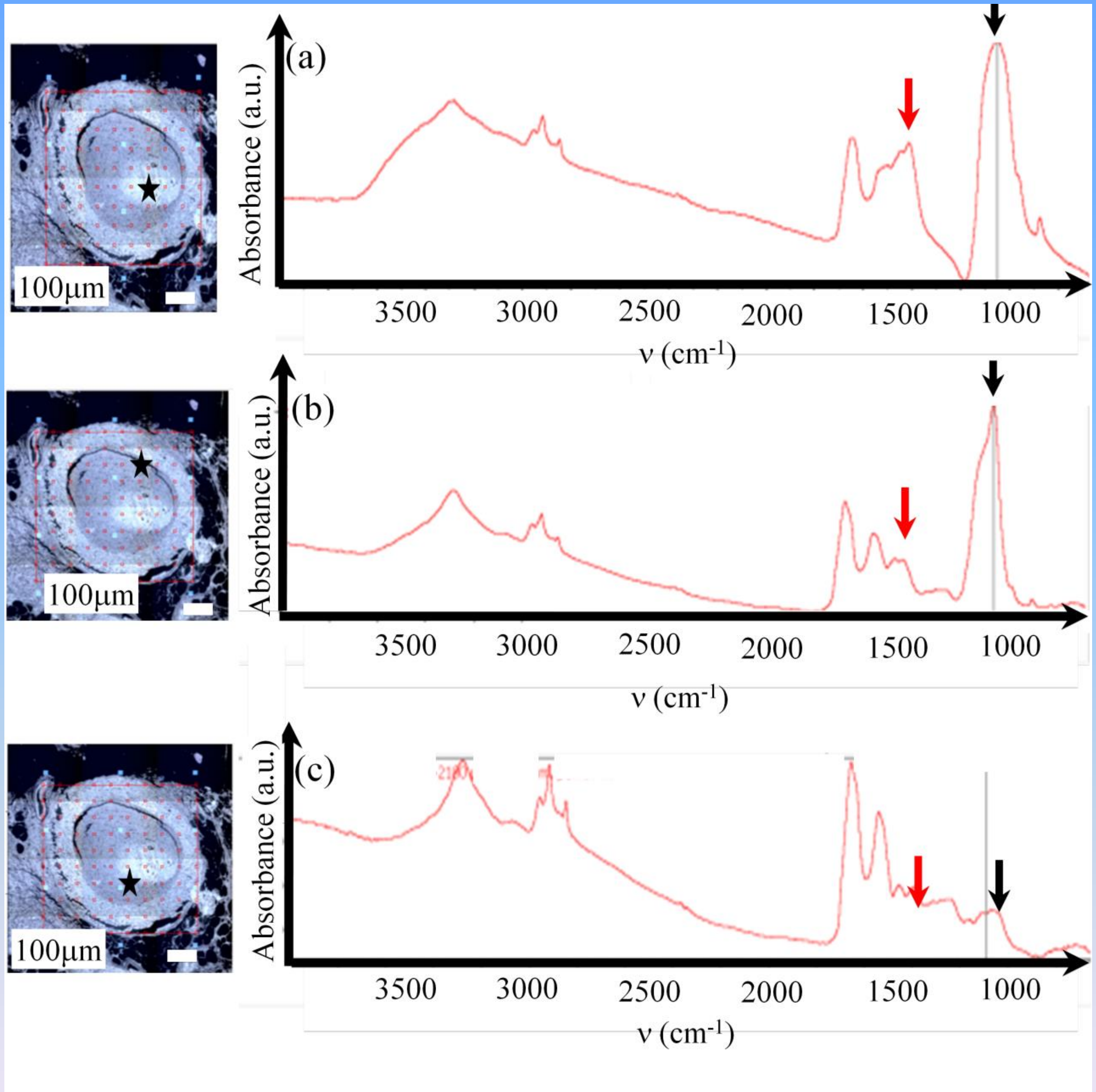



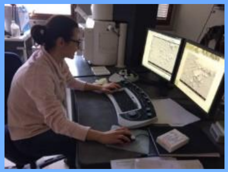
# Taux de Carbonate → Gradient de Carbonate

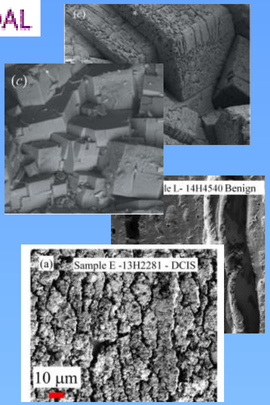



Nouvelle phase chimique identifiée : Phosphate de calcium apatitique amorphe



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